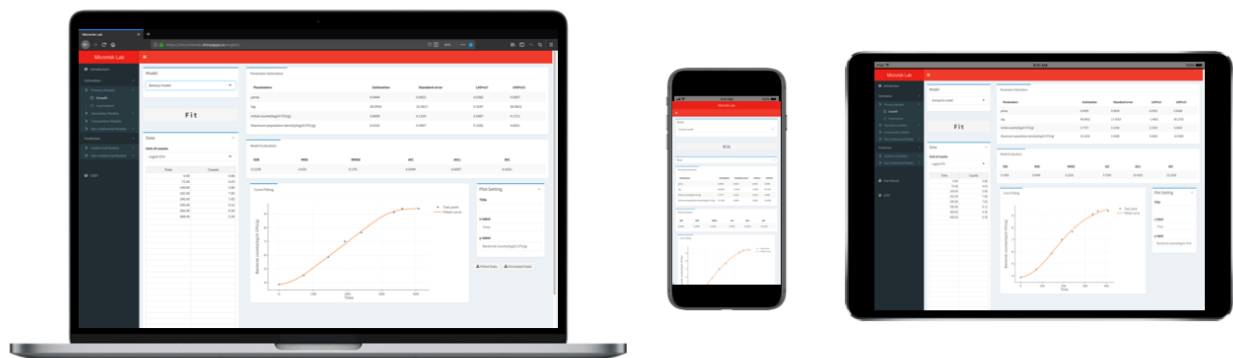


Microrisk Lab

User Manual

Revised at February 2021

Version 1.2



Disclaimer and Support

Disclaimer

Microrisk Lab and this manual provide NO WARRANTY. This tool is free to use but only for research purposes. It is not permitted to include Microrisk Lab in any other application. We would very appreciate acknowledgement if the tool is used.

Feedback

If you have any suggestion or for technical questions for Microrisk Lab, please contact the developer and maintainer Yangtai Liu (usstlyt@163.com), Your comments are highly appreciated.

Document Revisions

Date	Version	Document Changes
01/09/2017	Beta 0.1	Initial draft
01/01/2018	1.0	Draft for updated version
09/29/2019	1.1	Revised draft
02/20/2021	1.2	Revised draft

Contents

Disclaimer and Support	2
1 List of symbols	4
2 Unit	5
3 Programing basics	5
4 Functions included in Microrisk Lab.....	6
5 Layout of Microrisk Lab.....	7
6 Estimation module of Microrisk Lab	8
<i>Practical example I - Isothermal growth fitting.....</i>	<i>8</i>
7 Simulation module of Microrisk Lab	20
<i>Practical example II- Stochastic growth simulation</i>	<i>20</i>
8 Predictive models integrated in Microrisk Lab.....	25
9 Statistical indicators in Microrisk Lab.....	29
Reference	30

1 List of symbols

$Y(t), Y_0, Y_{max}$	the natural logarithm of real-time, initial, and maximum bacterial counts (ln CFU/g).
$y(t), y_0, y_{max}$	the 10-base logarithm of real-time, initial, and maximum bacterial counts (log10 CFU/g).
y_{res}	the 10-base logarithm of the residual bacterial counts (log10 CFU/g).
μ_{max}, μ_{opt}	the maximum and optimal specific growth rate.
k_{max}	the maximum specific inactivation rate.
D	the time of decimal reduction in inactivation.
D_{ref}	the referenced decimal reduction time at T_{ref} .
t_{lag}	the time of lag in growth.
S_l	the time of shoulder (or before inactivation) in inactivation.
t	the observed time.
t_{max}	the time when entering the stationary phase in growth.
S_t	the time when entering the stationary phase in inactivation.
T, pH, aw	The temperature (°C), pH, and water activity at t .
$T_{min}, T_{opt}, T_{max}$	the minimum, optimal, and maximum growth temperature (°C).
T_{ref}	the referenced inactivation temperature (°C).
$pH_{min}, pH_{opt}, pH_{max}$	the minimum, optimal, and maximum growth pH.
$aw_{min}, aw_{opt}, aw_{max}$	the minimum, optimal, and maximum growth water activity.
q_0	the initial physiological state of the inoculum in the Baranyi model.
δ, p	the coefficients in the Weibull model.
δ_{ref}	the referenced δ value at T_{ref} .
a, b	the coefficients in the square-root model.
A, m	the coefficients in the dynamic Huang model.
z	the coefficients of the bacterial thermal resistance (°C).

2 Unit

The unit of the bacterial count and time related variables can be defined by the user. The unit of predicted counting outputs will be transferred into 10-base logarithm. Note that the unit of the specific (growth/ inactivation) rate is a natural logarithm combined with a unit of time, for example, $\ln \text{CFU/g/h}$ or $\ln \text{CFU/g/min}$.

3 Programing basics

Microrisk Lab is developed by the open-source language R (version 3.5.1 for Mac OS X; <http://www.r-project.org>). All users are free to access and use this tool through the browser of any internet-connected device by the following links:

<http://microrisklab.shinyapps.io/english> (in English)

<http://microrisklab.shinyapps.io/chinese> (in Chinese)

The operation of this Microrisk Lab must depend on certain developed R packages, which were listed in Tab.1. All the required packages have been hosted and deployed in the Shinyapps.io sever (<https://www.shinyapps.io>).

Tab.1 Imported R packages in Microrisk Lab

Package name	Version	Reference	Purpose
<i>ggplot2</i>	3.3.1	Wickham et al.	to generate visualized plots for output
<i>mc2d</i>	0.1-18	Pouillot et al.	to generate certain distribution for output
<i>Metrics</i>	0.1.4	Hamner et al.	to calculate statistical indicators for output
<i>plotly</i>	4.9.0	Sievert et al.	to generate interactive plots for output
<i>rhandsontable</i>	0.3.7	Owen et al.	to build interactive table for input
<i>shiny</i>	1.0.5	Chang et al.	to establish and upload the shiny app
<i>shinyalert</i>	1.0	Attali et al.	to pop the error alert for input and output
<i>shinydashboard</i>	0.7.1	Chang et al.	to build the interactive interface
<i>shinyWidgets</i>	0.4.8	Perrier et al.	to build the interactive interface
<i>stats</i>	3.4.3	-	to realize the regression analysis

Microrisk Lab can be also used on computers without internet connection when installed locally. In this case, please contact the developer.

4 Functionalities included in Microrisk Lab

Microrisk Lab includes the following functions:

- Kinetic analysis of microbial isothermal growth
- Kinetic analysis of microbial non-isothermal growth
- Kinetic analysis of microbial isothermal inactivation
- Kinetic analysis of microbial non-isothermal inactivation
- Kinetic analysis of two-flora isothermal competition growth
- Secondary modeling of specific growth rate vs. temperature, pH and A_w .
- Deterministic/ Stochastic simulation for microbial isothermal growth
- Deterministic simulation for microbial isothermal growth
- Deterministic/ Stochastic simulation for microbial isothermal inactivation
- Deterministic simulation for microbial isothermal inactivation
- Output interactive plots of the fitted and predicted curve.
- Output estimated results (estimates, standard error, and 95% confidential intervals) and multiple statistical indicators (RSS, MSE, RMSE, AIC, AICc, BIC, R^2 , and Adjusted R^2) with respect to the experimental data in the 'Estimation' module.
- Output simulated bacterial counts or the distribution of the specific rate and final bacterial counts in the 'Simulation' module.
- Output correlation analysis between model parameters and simulated bacterial counts in the stochastic simulation.

5 Layout of Microrisk Lab

Fig.1 shows the page structure when loading in the Microrisk Lab via the browser in different devices. Users may switch the task by the main menu on the left side. In the setting panel, user can input the experimental data and choose the model here. The result panel will provide the estimated (predicted) values, statistical results, and interactive plots according to the setting.

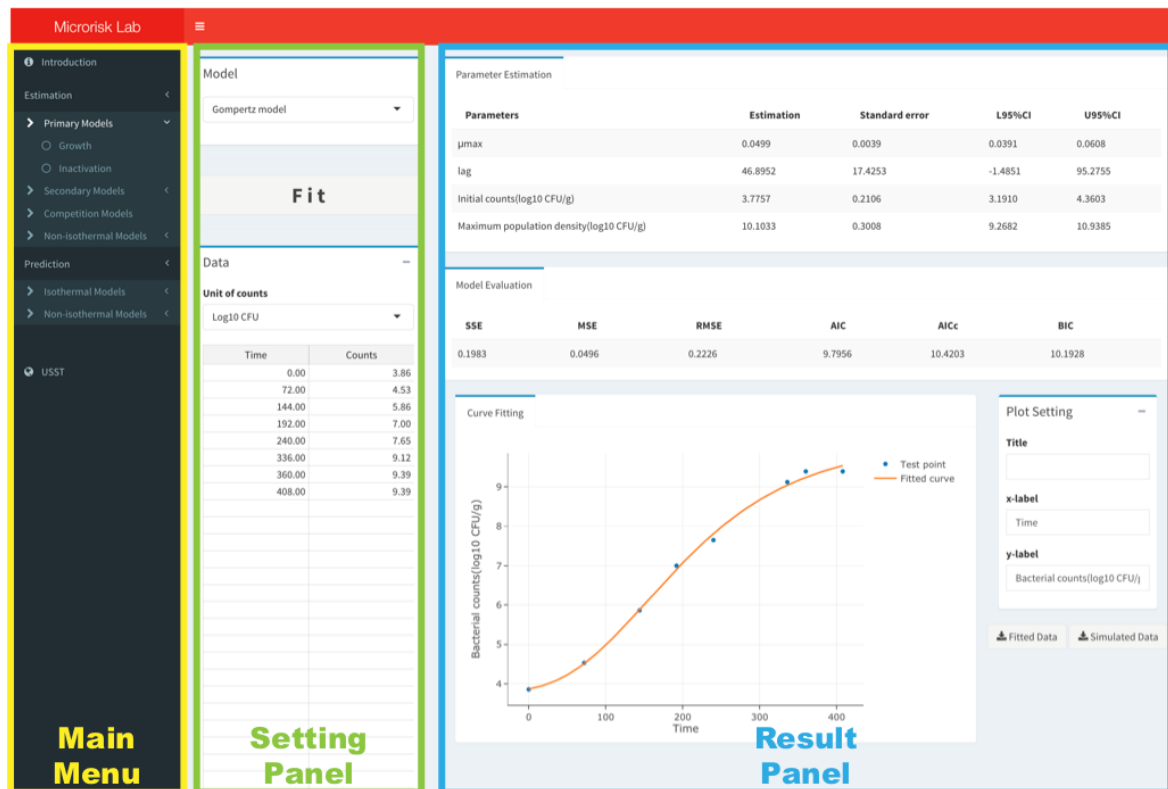


Fig.1 Typical layout of Microrisk Lab.

6 Estimation module of Microrisk Lab

The estimation module allows to solve multiple inverse problems in predictive microbiology, including ① isothermal growth fitting, ② isothermal inactivation fitting, ③④⑤ secondary model fitting, ⑥ two flora competition growth fitting, ⑦ non-isothermal growth fitting, and ⑧ non-isothermal inactivation fitting (Fig.2).

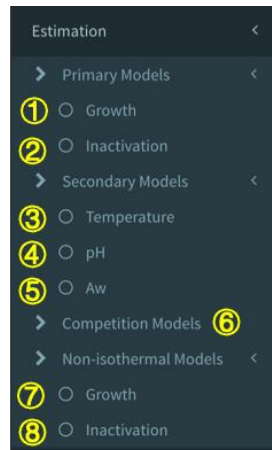


Fig.2 Different sections of model fitting in the estimation module.

Practical example I - Isothermal growth fitting

- (1) In this case, a group of *Listera monocytogenes/ innocua* growth in tryptose phosphate broth (TPB) obtained from the ComBase database (www.combase.cc, ComBase ID: LM127_11) was used as the test dataset for the growth fitting.
- (2) Choose ① the 'Growth' in the section of the 'Primary Models', and the setting panel of isothermal growth model will show up (Fig.3).

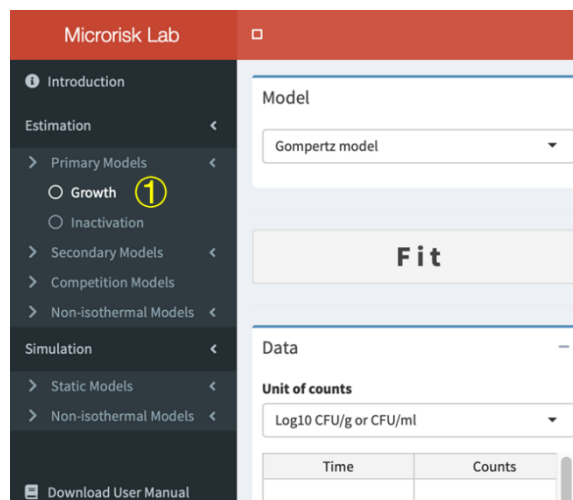


Fig.3 Layout of a section of the 'Estimation' module.

- (3) The experimental data can be ① directly typed (or ② copied from other table files) in the ‘Data’ box. Specifically, ③ the unit of bacterial counts should be confirmed by the user. If the inputted observations are more than 30, please ④ right click the mouse or ⑤ drag the last column to add additional columns (Fig.4).

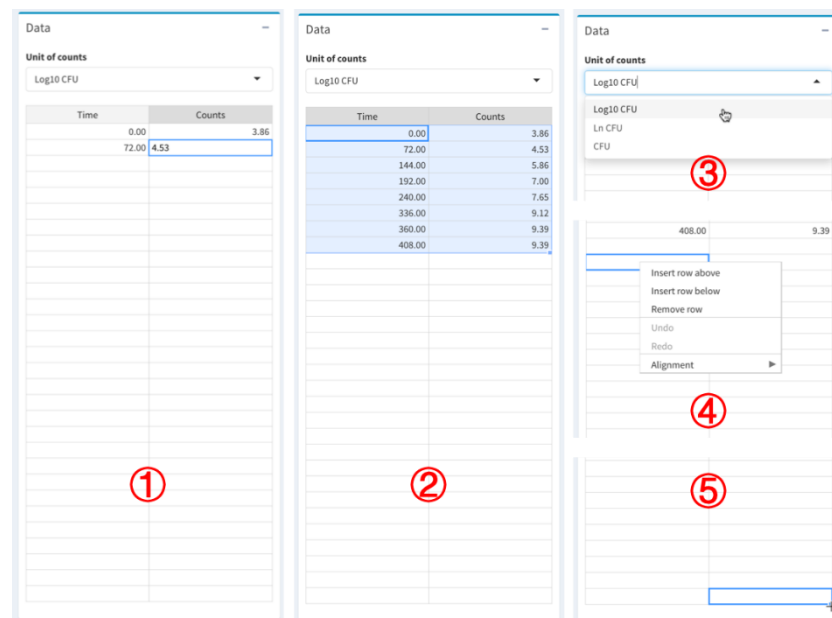


Fig.4 Boxes for the data input and unit selection.

- (4) After entering the data for model fitting, the growth model can be selected in the ‘Model’ list (Fig.5).

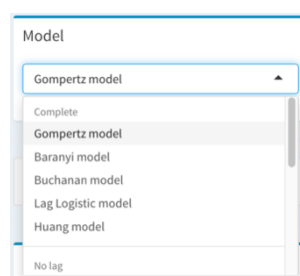
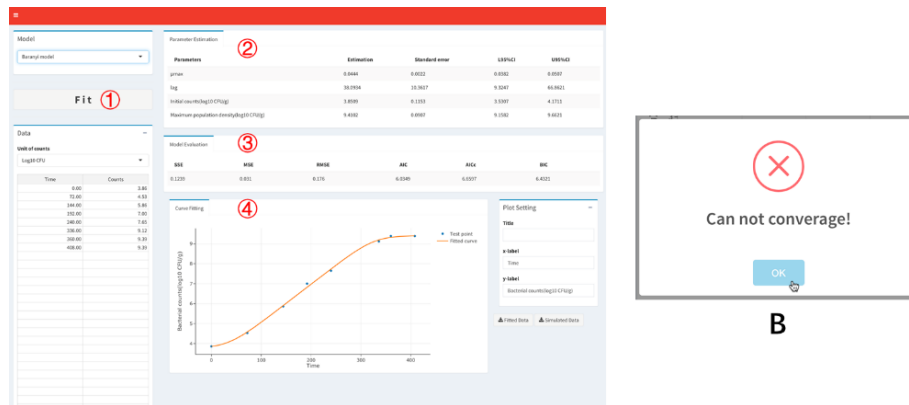


Fig.5 Box for the growth model selection

- (5) Click ① the ‘Fitting’ button. After a necessary loading time, if the regression can be solved successfully, the ② estimated result, ③ evaluated result, and ④ interactive plot of the observation and fitted curve will show in the result panel (Fig.6A). Otherwise, a popup message will appear for the regression warning, which means that the non-linear regression is failed (Fig.6B). In this case, please re-check the unit of bacterial counts and the model selection.



A
Fig.6 Layout of the interface after model fitting.

(6) The observed and predicted value can be viewed on ① the interactive plot. The observed data or fitting curve can be omitted from the plot by clicking ② the legend. Meanwhile, it is easy to edit the axis detail (③ the range and ④ title) of the interactive plot in real-time by ⑤ the box of 'Plot Setting'. After all, the plot is adjustable and downloadable by using ⑥ the 'Plotly toolbox'. Meanwhile, ⑦ the fitted and simulated data can be saved as the '.csv' file for comparison and further model development (Fig.7).

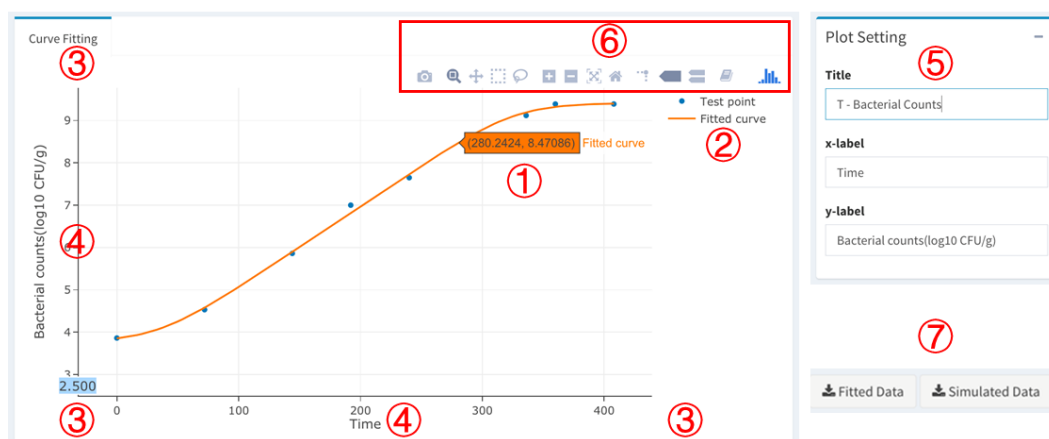


Fig.7 The interactive plot and the editorial box.

(7) For this case, the estimated result of parameters by using different growth models are listed in Tab.1, Tab.2, and Tab.3.

Tab.1 Static growth fitting results of the complete model in Microrisk Lab

Gompertz			Baranyi		Buchanan		Lag Logistic		Huang	
Parameter estimation*										
Parameters	Est. (95% CI) **	SE	Est. (95% CI) **	SE	Est. (95% CI) **	SE	Est. (95% CI) **	SE	Est. (95% CI) **	SE
y_0 (log10 CFU/g)	3.78 (3.19, 4.36)	0.21	3.85 (3.53, 4.17)	0.12	3.86 (3.44, 4.28)	0.15	3.86 (3.53, 4.17)	0.11	3.86 (3.55, 4.17)	0.11
y_{max} (log10 CFU/g)	10.10 (9.27, 10.94)	0.30	9.41 (9.16, 9.66)	0.09	9.30 (9.06, 9.54)	0.09	9.42 (9.16, 9.66)	0.09	9.42 (9.18, 9.66)	0.09
t_{lag} (h)	46.90 (-1.49, 95.28)	17.43	38.09 (9.32, 66.86)	10.36	36.01 (3.06, 68.97)	11.87	35.52 (9.32, 66.86)	8.59	35.52 (11.69, 59.36)	8.59
μ_{max} (1/h)	0.050 (0.04, 0.06)	0.004	0.044 (0.038, 0.051)	0.002	0.044 (0.036, 0.052)	0.003	0.044 (0.038, 0.051)	0.002	0.044 (0.039, 0.049)	0.00
Model evaluation										
RSS	0.4566		0.2853		0.0897		0.2598		0.2598	
MSE	0.1141		0.0713		0.0224		0.0649		0.0649	
RMSE	0.3379		0.2671		0.1497		0.2548		0.2548	
AIC	7.7956		4.0349		-5.2237		3.2840		3.2840	
AICc	13.1289		9.3683		0.1096		8.6173		8.6173	
BIC	8.1133		4.3527		-4.9059		3.6018		3.6018	

* Est.: Estimation; SE: Standard error.

** 95%CI: lower and upper 95% confidence intervals.

Tab.2 Static growth fitting results of the no lag model and linear model in Microrisk Lab

	No lag Logistic		No lag Buchanan		Linear	
Parameter estimation*						
Parameters	Est. (95% CI) **	SE	Est. (95% CI) **	SE	Est. (95% CI) **	SE
y_0 (log10 CFU/g)	3.60 (3.18, 4.02)	0.16	3.65 (3.27, 4.03)	0.15	3.81 (3.25, 4.37)	0.23
y_{max} (log10 CFU/g)	9.51 (8.98, 10.04)	0.21	9.39 (9.02, 9.76)	0.14	- -	-
μ_{max} (1/h)	0.039 (0.033, 0.045)	0.002	0.038 (0.033, 0.042)	0.002	0.035 (0.030, 0.040)	0.002
Model evaluation						
R ²	-		-		0.9793	
Adjusted R ²	-		-		0.9751	
RSS	1.1793		0.2037		0.3017	
MSE	0.2359		0.0407		0.0503	
RMSE	0.4857		0.2019		0.2242	
AIC	13.3871		-0.6606		7.1519	
AICc	13.3871		-0.6606		5.5519	
BIC	13.6254		-0.4222		7.3108	

* Est.: Estimation; SE: Standard error.

** 95%CI: lower and upper 95% confidence intervals.

Tab.3 Static growth fitting results of the reduced model in Microrisk Lab

Reduced Baranyi			Reduced Buchanan		Reduced Huang	
Parameter estimation*						
Parameters	Est. (95% CI) **	SE	Est. (95% CI) **	SE	Est. (95% CI) **	SE
y_0 (log10 CFU/g)	3.83 (2.90, 4.82)	0.37	3.86 (3.53, 4.17)		3.86 (3.53, 4.17)	
t_{lag} (h)	2.13 (-78.88, 90.42)	32.93	5.77 (9.32, 66.86)	8.59	5.77 (9.32, 66.86)	8.59
μ_{max} (1/h)	0.035 (0.028, 0.042)	0.003	0.035 (0.038, 0.051)		0.035 (0.038, 0.051)	
Model evaluation						
RSS	3.6796		0.6904		3.6605	
MSE	0.7359		0.1381		0.7321	
RMSE	0.8579		0.3716		0.8556	
AIC	22.4900		9.1037		22.4482	
AICc	22.4900		9.1037		22.4482	
BIC	22.7283		9.3420		22.6865	

* Est.: Estimation; SE: Standard error.

** 95% CI: lower and upper 95% confidence intervals.

Practical example II - Isothermal inactivation fitting

- (1) In this case, a group of *Escherichia coli* inactivation in broth with 5% ethanol and 11200 ppm lactic acid (pH=3.8) at 5°C obtained from the ComBase database (ComBase ID: CA_Ec025) was used as the test dataset for the inactivation fitting.
- (2) Choose the ② 'Inactivation' in the section of the 'Primary Models' (see Fig.2), and the setting panel of isothermal inactivation model will show up. The steps of importing data and obtaining results are similar to the isothermal growth fitting (see Fig.4 to Fig.7).
- (3) For this case, the estimated result of parameters by using different growth model are listed in Tab.4, Tab.5 and Tab.6.

Tab.4 Static inactivation fitting results of the Geeraerd model in Microrisk Lab

	Complete Geeraerd		No shoulder Geeraerd		No tail Geeraerd	
Parameter estimation*						
Parameters	Est. (95% CI) **	SE	Est. (95% CI) **	SE	Est. (95% CI) **	SE
y_o (log10 CFU/g)	8.97 (6.37, 11.56)	0.20	9.10 (8.24, 9.97)	0.20	9.02 (7.86, 10.18)	0.27
y_{res} (log10 CFU/g)	6.71 (3.42, 9.99)	0.26	6.52 (4.34, 8.71)	0.51	- -	-
S_l (h)	1.65 (-11.56, 14.86)	1.04			-0.01 (-8.44, 8.41)	1.96
k_{max} (1/h)	1.184 (-3.944, 6.311)	0.404	0.805 (0.099, 1.511)	0.164	0.690 (-0.084, 1.464)	0.180
Model evaluation						
RSS	0.0429		0.1047		0.1480	
MSE	0.0429		0.0523		0.0740	
RMSE	0.2071		0.2288		0.2720	
AIC	-1.6056		0.8567		2.5894	
AICc	-		18.8567		20.5894	
BIC	-3.1678		-0.3150		1.4177	

* Est.: Estimation; SE: Standard error.

** 95%CI: lower and upper 95% confidence intervals.

Tab.5 Static inactivation fitting results of the three/ two phase model in Microrisk Lab

Three-phase			No shoulder two-phase		No tail two-phase	
Parameter estimation*						
Parameters	Est. (95% CI) **	SE	Est. (95% CI) **	SE	Est. (95% CI) **	SE
y_0 (log10 CFU/g)	9.00 (6.93, 11.07)	0.16	9.11 (8.45, 9.77)	0.15	9.00 (7.83, 10.17)	0.27
y_{res} (log10 CFU/g)	6.80 (4.73, 8.87)	0.16	6.80 (6.01, 7.59)	0.18	- -	-
S_l (h)	0.92 (-7.32, 9.15)	0.65	- -	-	0.16 (-5.78, 6.11)	1.38
k_{max} (1/h)	0.921 (-0.768, 2.610)	0.133	0.794 (0.389, 1.200)	0.094	0.702 (0.102, 1.303)	0.140
Model evaluation						
RSS	0.0267		0.0670		0.1470	
MSE	0.0267		0.0335		0.0735	
RMSE	0.1633		0.1830		0.2711	
AIC	-3.9795		-1.3731		2.5556	
AICc	-		16.6269		20.5556	
BIC	-5.5418		-2.5448		1.3839	

* Est.: Estimation; SE: Standard error.

** 95%CI: lower and upper 95% confidence intervals.

Tab.6 Static inactivation fitting results of the Weibull model and Bigelow model in Microrisk Lab

	Webull-tail		Webull		Bigelow	
Parameter estimation*						
Parameters	Est. (95% CI) **	SE	Est. (95% CI) **	SE	Est. (95% CI) **	SE
y_0 (log10 CFU/g)	8.96 (6.94, 10.97)	0.16	9.04 (7.89, 10.19)	0.27	9.02 (8.47, 9.57)	0.17
y_{res} (log10 CFU/g)	8.96 (4.53, 8.98)	0.18	- -	-		
p	1.73 (-5.05, 8.51)	0.53	3.21 (-1.58, 8.00)	1.11		
δ	3.63 (-2.65, 9.90)	0.49	0.96 (-0.38, 2.30)	0.31		
D (h)	- -	-	- -	-	3.33 (2.09, 4.58)	0.39
Model evaluation						
R ²	-		-		0.9605	
Adjusted R ²	-		-		0.9408	
RSS	0.0271		0.1467		0.1480	
MSE	0.0271		0.0733		0.0493	
RMSE	0.1648		0.2708		0.2221	
AIC	-3.8901		2.5449		0.5895	
AICc	-		20.5449		2.5895	
BIC	-5.4524		1.3732		-0.1916	

* Est.: Estimation; SE: Standard error.

** 95%CI: lower and upper 95% confidence intervals.

Practical example III - Temperature secondary model fitting

- (1) In this case, a study on the maximum specific growth rate of *Salmonella* Typhimurium (ATCC 14028) in chicken breast (Oscar, 2002) was cited for fitting different secondary models.
- (2) Choose the ③ ‘Temperature’ in the section of the ‘Secondary Models’ (see Fig.2), and the setting panel of temperature secondary model will show up. The steps of importing data and obtaining results are similar to the isothermal growth fitting (see Fig.4 to Fig.7).
- (3) For this case, the estimated result of parameters by using different temperature secondary model are listed in Tab.7 and Tab.8.

Tab.7 Specific maximum growth rate fitting results of the suboptimal temperature secondary model
in Microrisk Lab

Square-root model			Huang square-root model	
Parameter estimation*				
Parameters	Est. (95% CI) **	SE	Est. (95% CI) **	SE
a	0.018 (0.010, 0.027)	0.004	0.063 (0.044, 0.082)	0.009
T_{min} (°C)	-21.17 (-45.65, 3.31)	11.70	-7.17 (-23.51, 9.18)	7.81
Model evaluation				
RSS	2.5196		2.3500	
MSE	0.1326		0.1237	
RMSE	0.3642		0.3517	
AIC	19.0665		17.6036	
AICc	15.7332		14.2703	
BIC	21.1556		19.6926	

* Est.: Estimation; SE: Standard error.

** 95%CI: lower and upper 95% confidence intervals.

Tab.8 Specific maximum growth rate fitting results of the full temperature secondary model in
Microrisk Lab

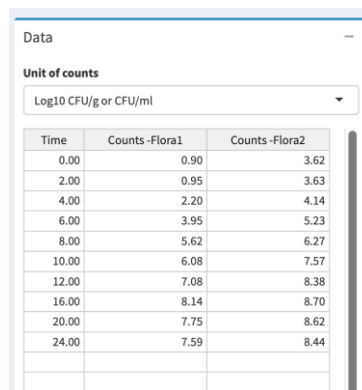
	Square-root model		Huang square-root model		Cardinal parameter model	
Parameter estimation*						
Parameters	Est. (95% CI) **	SE	Est. (95% CI) **	SE	Est. (95% CI) **	SE
a	0.043 (0.036, 0.051)	0.004	0.087 (0.077, 0.098)	0.005	- -	-
b	0.15 (0.09, 0.20)	0.02	0.79 (0.60, 0.99)	0.09	- -	-
T_{min} (°C)	4.09 (0.88, 7.31)	1.52	3.59 (-0.78, 7.97)	2.08	5.56 (3.02, 8.10)	1.21
T_{max} (°C)	51.89 (50.55, 53.23)	0.63	47.49 (47.35, 47.63)	0.07	49.59 (48.88, 50.30)	0.336
μ_{opt} (1/h)	- -	-	- -	-	1.621 (1.559, 1.682)	0.029
T_{opt} (°C)	- -	-	- -	-	39.76 (38.96, 40.56)	0.38
Model evaluation						
RSS	0.0999		0.3851		0.0811	
MSE	0.0059		0.0227		0.0048	
RMSE	0.0767		0.1505		0.0691	
AIC	-44.7130		-16.3782		-48.1028	
AICc	-50.2130		-21.8782		-54.6028	
BIC	-40.5349		-12.2001		-44.9248	

* Est.: Estimation; SE: Standard error.

** 95%CI: lower and upper 95% confidence intervals.

Practical example IV - Two flora competition growth fitting

- (1) In this case, a study on the competition growth of *Escherichia coli* O157:H7 in ground beef and the background microflora (Vimont et al., 2006) was cited for fitting. Note that the dataset was obtain from the R package ‘*nlsMicrobio*’ (Baty & Delignette-Muller, 2015).
- (2) Choose the ⑥ section of the ‘Competition Models’ (see Fig.2), and the setting panel of the competition growth model will show up. The steps of importing data and obtaining results are similar to the isothermal growth fitting (see Fig.4 to Fig.7). While the counting data of the two flora should be input together in the ‘Data’ box (Fig.8).



Time	Counts-Flora1	Counts-Flora2
0.00	0.90	3.62
2.00	0.95	3.63
4.00	2.20	4.14
6.00	3.95	5.23
8.00	5.62	6.27
10.00	6.08	7.57
12.00	7.08	8.38
16.00	8.14	8.70
20.00	7.75	8.62
24.00	7.59	8.44

Fig.8 Box for the competition growth data input.

- (3) For this case, the estimated result of parameters by using different temperature secondary model are listed in Tab.9.

Tab.9 Two flora growth fitting results of the competition model in Microrisk Lab

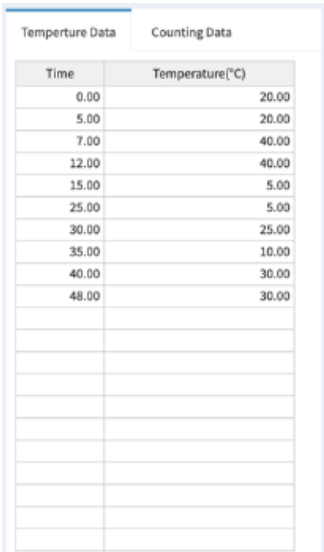
	Jameson-No lag Buchanan model		Jameson-Buchanan model	
Parameter estimation*				
Parameters	Est. (95% CI) **	SE	Est. (95% CI) **	SE
μ_{max} (1/h) - Flora 1	1.323 (1.150, 1.467)	0.081	1.566 (1.360, 1.771)	0.10
μ_{max} (1/h) - Flora 2	1.001 (0.842, 1.160)	0.075	1.323 (1.075, 1.571)	0.115
y_0 (log10 CFU/g) - Flora 1	0.38 (-0.21, 0.96)	0.27	0.90 (0.26, 1.55)	0.30
y_0 (log10 CFU/g) - Flora 2	2.94 (2.37, 3.52)	0.27	3.63 (3.17, 4.08)	0.21
t_{lag} (h) - Flora 1			1.80 (0.60, 3.00)	0.55
t_{lag} (h) - Flora 2			3.20 (1.91, 4.48)	0.59
t_{max} (h)	12.97 (11.81, 14.13)	0.54	11.73 (10.87, 12.58)	0.40
Model evaluation				
RSS	2.5373		1.1581	
MSE	0.1692		0.0891	
RMSE	0.4113		0.2985	
AIC	25.4652		13.7782	
AICc	19.7509		9.1115	
BIC	30.4439		20.7483	

* Est.: Estimation; SE: Standard error.

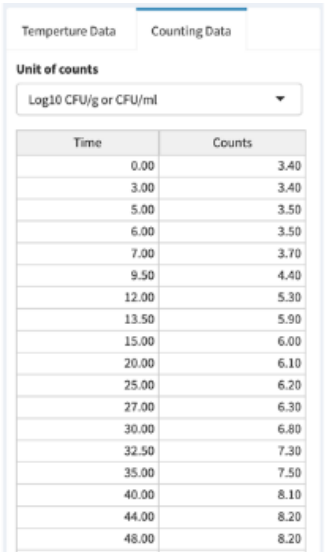
** 95%CI: lower and upper 95% confidence intervals.

Practical example V – Non-isothermal growth fitting


- (1) In this case, a study on the non-isothermal growth of *L. monocytogenes* in ready-to-eat braised beef was introduced for fitting two dynamic growth models.
- (2) Choose the ⑦ ‘Growth’ in the section of the ‘Non-isothermal Models’ (see Fig.2), and the setting panel of temperature secondary model will show up.
- (3) Both time-temperature profile and the bacterial counting data are required in the non-isothermal modeling (Fig. 9A and Fig. 9B). Meanwhile, the initial guess of the model parameter was also necessary to conduct the regression (Fig. 9C). User can also change the time-step of the regression (default is 0.1). Then the estimated results should be listed if the converge is successful.



A



B



C

Fig.9 Box for (A) temperature profile and (B) input; and (B) the setting of initial guesses.

- (4) For this case, the estimated result of parameters by using two non-isothermal growth model are listed in Tab.10.

Tab.10 Non-isothermal growth fitting results of the dynamic model in Microrisk Lab

Baranyi-Cardinal parameter model				Huang-Cardinal parameter model			
Parameter estimation*							
Parameters	Int.	Est. (95% CI) **	SE	Parameters	Int.	Est. (95% CI) **	SE
y_0 (log10 CFU/g)	-	3.39 (3.36, 3.43)	0.02	y_0 (log10 CFU/g)	-	3.45 (3.41, 3.50)	0.02
y_{max} (log10 CFU/g)	-	8.21 (8.18, 8.25)	0.02	y_{max} (log10 CFU/g)	-	8.21 (8.16, 8.27)	0.03
μ_{opt} (1/h)	1	1.065 (0.854, 1.276)	0.096	μ_{opt} (-h)	1	1.242 (0.825, 1.659)	0.187
T_{opt} (°C)	37	36.4 (35.4, 37.5)	0.5	T_{opt} (°C)	37	38 (33.5, 42.4)	2
T_{min} (°C)	0	-1.1 (-2.6, 0.5)	0.7	T_{min} (°C)	0	-2.8 (-7.4, -1.8)	2.1
T_{max} (°C)	45	42.4 (38.4, 46.4)	1.8	T_{max} (°C)	45	40.3 (38.7, 41.9)	0.7
q_0	1	0.0244 (0.0167, 0.0321)	0.0035	A	1	1.91 (1.84, 1.99)	0.04
				m	1	0.33 (0.17, 0.48)	0.07
Step size (h)				0.1			
Model evaluation							
RSS	0.0071				0.0155		
MSE	0.0006				0.0016		
RMSE	0.0253				0.0394		
AIC	-46.0602				-29.8674		
AICc	-48.8602				-29.8674		
BIC	-39.8276				-22.7444		

* Int.: Initial guess; Est.: Estimation; SE: Standard error.

** 95% CI: lower and upper 95% confidence intervals.

Practical example VI – Non-isothermal inactivation fitting

- (1) In this case, a study on the non-isothermal inactivation of *Bacillus sporothermodurans* IC4 spores under dynamic heating conditions (Garre et al, 2018) was cited for fitting two dynamic inactivation models.
- (2) Choose the ⑧ ‘Inactivation’ in the section of the ‘Non-isothermal Models’ (see Fig.2), and the setting panel of temperature secondary model will show up. The steps of importing data and obtaining results are similar to the non-isothermal growth fitting (see Fig. 9).
- (3) For this case, the estimated result of parameters by using two non-isothermal inactivation model are listed in Tab.11.

Tab.11 Non-isothermal inactivation fitting results of the dynamic model in Microrisk Lab

Dynmaic Bigelow model				Dynamic Weibull model			
Parameter estimation*							
Parameters	Int.	Est. (95% CI) **	SE	Parameters	Int.	Est. (95% CI) **	SE
$T_{ref} (^{\circ}\text{C})$	130	- -	-	$T_{ref} (^{\circ}\text{C})$	130	- -	-
y_0 (log10 CFU/g)	-	5.78 (5.69, 5.87)	0.04	y_0 (log10 CFU/g)	-	5.78 (5.69, 5.88)	0.04
D_{ref} (min)	2	0.18 (0.05, 0.31)	0.06	δ_{ref}	2.00	4.88 (-8.72, 18.48)	6.42
z ($^{\circ}\text{C}$)	6	6.67 (4.7, 8.6)	0.92	z ($^{\circ}\text{C}$)	6.00	9.79 (-3.52, 23.09)	6.28
				p	1.00	1.35 (0.01, 2.69)	0.63
Step size (h)				0.01			
Model evaluation							
RSS	0.1737			0.1704			
MSE	0.0102			0.0106			
RMSE	0.1011			0.1032			
AIC	-32.1667			-30.5504			
AICc	-36.6667			-35.8837			
BIC	-29.1795			-26.5675			

* Int.: Initial guess; Est.: Estimation; SE: Standard error.

** 95%CI: lower and upper 95% confidence intervals.

7 Simulation module of Microrisk Lab

The simulation module allows to solve the ①② isothermal and ③④ non-isothermal forward problem in predictive microbiology (Fig.10). There are no limitations in the condition setting. Users may simulate the bacterial growth or inactivation with the prior knowledge on the kinetic parameter and growth/ death boundary. Moreover, both deterministic and stochastic models are provided in the isothermal simulation.



Fig.10 Different sections of model fitting in the simulation module.

Practical example VII- Stochastic growth simulation

(1) The condition setting of the growth simulation is adopted from the stochastic growth of *Salmonella* Typhimurium individual cells researched by Koutsoumanis and Lianou (2013). Tab.12 lists the setting for simulation. The Buchanan model is chosen as the growth model for individual cells. A 10,000 times iteration was realized based on the simple sampling method for Monte-Carlo simulation.

Tab.12 Stochastic growth simulation settings for Microrisk Lab

Parameters	Microrisk Lab	
y_0 (log ₁₀ CFU/g)	Distribution	Normal
	Mean	0
	Standard deviation	0
y_{max} (log ₁₀ CFU/g)	Distribution	Normal
	Mean	8
	Standard deviation	0
t_{lag}	Distribution	LogNormal
	Mean	3.355
	Standard deviation	0.896
	Shift	-1.628
μ_{max}	Distribution	Logistic
	Mean	0.754
	Standard deviation	0.024
t	Distribution	Uniform
	Maximum	0
	Minimum	8
Model	Buchanan model	
Iteration times	10,000	

- (2) Choose ① the ‘Growth’ section of the ‘Isothermal Models’ in the ‘Simulation’ module, and ② choose ‘Stochastic’ model type in the setting panel (Fig.11). Then set the ③ ‘Iteration time’ and ④ ‘Model’ to ‘10,000’ and ‘Buchanan model’, respectively.

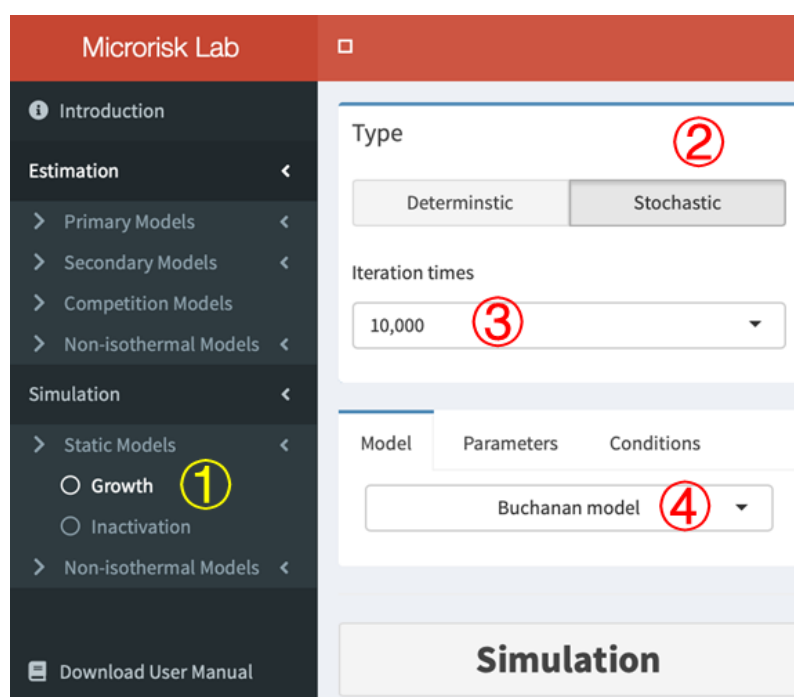


Fig.11 Layout of a section of the ‘Simulation’ module.

- (3) Switch to the ① ‘Parameters’ tab to determine the setting of the (distribution of) ② y_{max} , ③ t_{lag} , and ④ μ_{max} according to Tab.12 (Fig.12).

The screenshot shows the 'Parameters' tab of the Microrisk Lab software. The interface is divided into sections for different kinetic parameters. Red circles with numbers 1 through 4 highlight specific elements:

- ①: The 'Parameters' tab label.
- ②: The 'Maximum Population Density (log10 CFU/g)' section, which includes input fields for 'Mean' (8) and 'SD' (0).
- ③: The 'Lag' section, which includes a 'Distribution' dropdown set to 'Lognormal', and input fields for 'Mean' (3.355), 'SD' (0.896), and 'Shift' (-1.628).
- ④: The ' μ_{max} ' section, which includes a 'Distribution' dropdown set to 'Logistic', and input fields for 'Mean' (0.754) and 'SD' (0.024).

Fig.12 Box for kinetic parameter setting.

- (4) Switch to the ① ‘Conditions’ tab to determine the setting of the (distribution of) ② y_0 , ③ t according to Tab.12 (Fig.13).

Fig.13 Box for condition setting.

- (5) Click the ① ‘Simulation’ button. After a necessary loading time, if no contradiction in the setting, the ② simulated curve/point and ③ predicted result will show in the result panel (Fig.14A). Otherwise, different popup messages will appear for the simulation warning (Fig.14B-D). In these cases, please check the setting of kinetic parameters and the condition of the simulated environment.



Fig.14 Layout of the interface after simulation.

- (6) The stochastic growth simulation can be viewed on ① the interactive plot, which is also adjustable and downloadable (Fig.15A). The distribution of ② the estimated μ_{max} and ③ final bacterial concentration (y_{final}), as well as ④ the estimated mean value and standard deviation will

be presented and listed (Fig.15B). The sensitivity analysis on model parameters is realized by calculating the Pearson correlation between different factors and the bacterial counts. Here, according to ⑤ the correlation plot, the duration of growth time is the most sensitive parameter for the bacterial counts during the stochastic growth of *S. Typhimurium* single cell (Fig.15B).

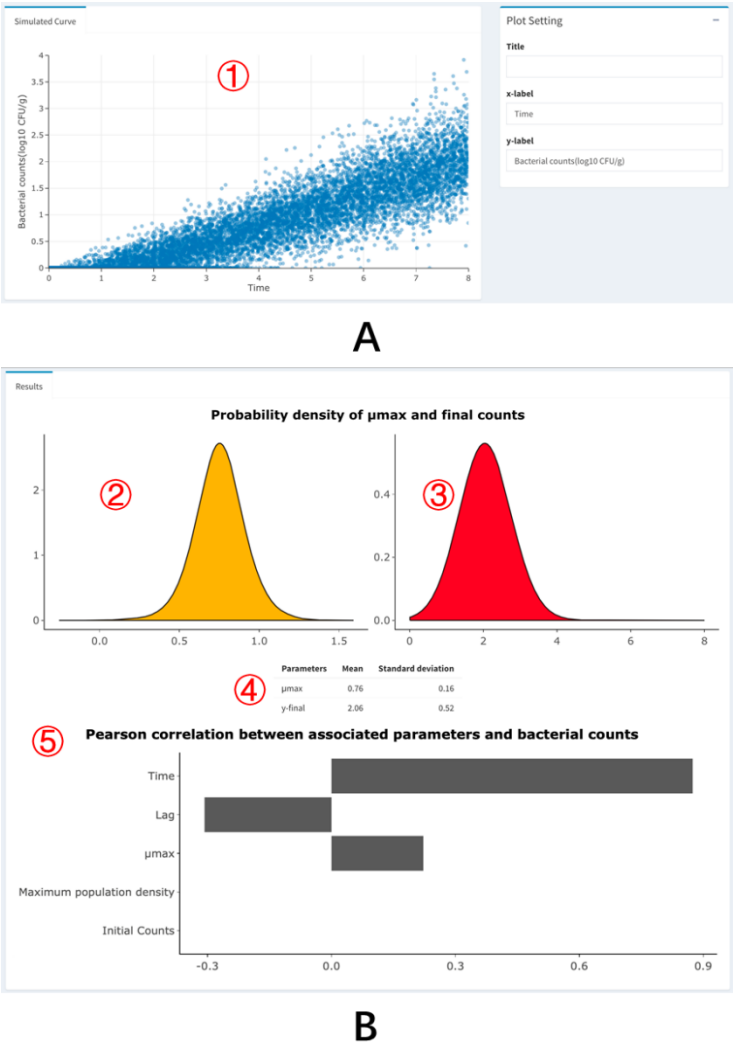


Fig.15 The result of stochastic simulation.

(7) Note that, in the section of ‘Non-isothermal Models’ of the simulation module, only deterministic model was provided in this version.

8 Predictive models integrated in Microrisk Lab

Microrisk Lab consists of 11 isothermal growth models (Tab.13), 9 inactivation models (Tab.14), 10 secondary models (Tab.15), 2 competition growth models (Tab.16), and 4 non-isothermal models (Tab.17) for estimation or simulation work.

Tab.13. Explicit equations for growth included in Microrisk Lab

Name	Formula
Complete model	
Gompertz model ¹	$Y(t) = Y_0 + (Y_{max} - Y_0) \exp \left\{ -\exp \left[\frac{2.71 \mu_{max} (t_{lag} - t)}{Y_{max} - Y_0} + 1 \right] \right\}$
Baranyi model ²	$\begin{cases} Y(t) = Y_0 + \mu_{max} A(t) - \ln \left[1 + \frac{\exp(\mu_{max} A(t)) - 1}{\exp(Y_{max} - Y_0)} \right] \\ A(t) = t + \frac{1}{\mu_{max}} \ln [\exp(-\mu_{max} t) + \exp(-\mu_{max} t_{lag}) - \exp(-\mu_{max} t - \mu_{max} t_{lag})] \end{cases}$
Buchanan model ³	$\begin{cases} y(t) = y_0, & t < t_{lag} \\ y(t) = y_0 + \frac{\mu_{max}}{\ln 10} (t - t_{lag}), & t_{lag} \leq t < t_{max} \\ y(t) = y_{max}, & t \geq t_{max} \end{cases}$
Lag-logistic model ⁴	$\begin{cases} Y(t) = Y_0, & t < t_{lag} \\ Y(t) = Y_{max} - \ln \{ 1 + [\exp(Y_{max} - Y_0) - 1] \exp[-\mu_{max} (t - t_{lag})] \}, & t \geq t_{lag} \end{cases}$
Huang model ⁵	$\begin{cases} Y(t) = Y_0 + Y_{max} - \ln \{ \exp(Y_0) + [\exp(Y_{max}) - \exp(Y_0)] \exp(-\mu_{max} B(t)) \} \\ B(t) = t + \frac{1}{4} \ln \frac{1 + \exp[-4(t - t_{lag})]}{1 - \exp(4t_{lag})} \end{cases}$
No lag model	
Logistic model ⁶	$Y(t) = Y_0 + Y_{max} - \ln \{ \exp(Y_0) + [\exp(Y_{max}) - \exp(Y_0)] \exp(-\mu_{max} t) \}$
Buchanan model ⁷	$\begin{cases} y(t) = y_0 + \frac{\mu_{max}}{\ln 10} t, & t < t_{max} \\ y(t) = y_{max}, & t \geq t_{max} \end{cases}$
Reduced model	
Baranyi model ⁸	$Y(t) = Y_0 + \mu_{max} t + \ln [\exp(-\mu_{max} t) + \exp(-\mu_{max} t_{lag}) - \exp(-\mu_{max} t - \mu_{max} t_{lag})]$
Buchanan model ⁹	$\begin{cases} y(t) = y_0, & t < t_{lag} \\ y(t) = y_0 + \frac{\mu_{max}}{\ln 10} (t - t_{lag}), & t \geq t_{lag} \end{cases}$
Huang model ¹⁰	$Y(t) = Y_0 + \mu_{max} t + \frac{1}{4} \mu_{max} \ln \frac{1 + \exp[-4(t - t_{lag})]}{1 - \exp(4t_{lag})}$
Linear model	
Linear model	$Y(t) = Y_0 + \mu_{max} t$

¹Zwietering et al., 1990; ^{2/8}Baranyi and Roberts, 1995; ^{3/7/9}Buchanan et al., 1997; ⁴Rosso et al., 1996; ^{5/6/10}Huang, 2008.

Tab.14. Explicit equations for inactivation included in Microrisk Lab

Name	Formula
Complete model	
Completed Geeraerd model ¹	$y(t) = y_{res} + \log_{10} \left[\frac{(10^{y_0 - y_{res}} - 1) \exp(k_{max} S_l)}{\exp(k_{max} t) + \exp(k_{max} S_l) - 1} + 1 \right]$
Three-phase model ²	$\begin{cases} y(t) = y_0, & t < S_l \\ y(t) = y_0 + \frac{k_{max}}{\ln 10} (t - S_l), & S_l \leq t < S_t \\ y(t) = y_{res}, & t \geq S_t \end{cases}$
Weibull-tail model ³	$y(t) = y_{res} + \log_{10} \left[(10^{y_0 - y_{res}} - 1) 10^{-\left(\frac{t}{\delta}\right)^p} + 1 \right]$
No shoulder model	
No shoulder Geeraerd model ⁴	$y(t) = y_{res} + \log_{10} \{ (10^{y_0 - y_{res}} - 1) \exp(k_{max} t) + 1 \}$
No shoulder two-phase model ⁵	$\begin{cases} y(t) = y_0 + \frac{k_{max}}{\ln 10} t, & t < S_t \\ y(t) = y_{res}, & t \geq S_t \end{cases}$
No tail model	
No tail Geeraerd model ⁶	$y(t) = y_0 + \frac{k_{max} t}{\ln 10} + \log_{10} \left\{ \frac{\exp(k_{max} S_l)}{1 + [\exp(k_{max} S_l) - 1] \exp(k_{max} t)} \right\}$
No tail two-phase model ⁷	$\begin{cases} y(t) = y_0, & t < S_l \\ y(t) = y_0 + \frac{k_{max}}{\ln 10} (t - S_l), & t \geq S_l \end{cases}$
Weibull model ⁸	$y(t) = y_0 - \left(\frac{t}{\delta} \right)^p$
Linear model	
Bigelow model ⁹	$y(t) = y_0 - \frac{t}{D}$

^{1/4/6} Geeraerd et al., 2000; ^{2/5/7} Buchanan and Golden, 1995; ³ Albert and Mafart, 2005; ⁸ van Boekel, 2002; ⁹ Bigelow, 1921.

Tab.15. Secondary models for μ_{max} included in Microrisk Lab

Name	Formula
Temperature models	
Suboptimal square-root model ¹	$\mu_{max} = [a(T - T_{min})]^2$
Full square-root model ²	$\mu_{max} = \langle a(T - T_{min})\{1 - \exp[b(T - T_{max})]\} \rangle^2$
Suboptimal Huang square-root model ³	$\mu_{max} = [a(T - T_{min})^{0.75}]^2$
Full Huang square-root model ⁴	$\mu_{max} = \langle a(T - T_{min})^{0.75}\{1 - \exp[b(T - T_{max})]\} \rangle^2$
Cardinal parameter model ⁵	$\mu_{max} = \frac{\mu_{opt}(T - T_{max})(T - T_{min})^2}{[(T_{opt} - T_{min})(T - T_{opt}) - (T_{opt} - T_{max})(T_{opt} + T_{min} - 2T)](T_{opt} - T_{min})}$
pH models	
Cardinal 3-parameter model ⁶	$\mu_{max} = \frac{\mu_{opt}(pH - pH_{min})[pH - (2pH_{opt} - pH_{min})]}{(pH - pH_{min})[pH - (2pH_{opt} - pH_{min})] - (pH - pH_{opt})^2}$
Cardinal 4-parameter model ⁷	$\mu_{max} = \frac{\mu_{opt}(pH - pH_{min})(pH - pH_{max})}{(pH - pH_{min})(pH - pH_{max}) - (pH - pH_{opt})^2}$
Quasi-mechanistic model ⁸	$\mu_{max} = \mu_{opt}(1 - 10^{pH_{min} - pH})$
Water activity models	
Cardinal 2-parameter model ⁹	$\mu_{max} = \frac{\mu_{opt}(aw - aw_{min})^2}{(1 - aw_{min})^2}$
Cardinal 3-parameter model ¹⁰	$\mu_{max} = \frac{\mu_{opt}(aw - 1)(aw - aw_{min})^2}{(aw_{opt} - aw_{min})[(aw_{opt} - aw_{min})(aw - aw_{opt}) - (aw_{opt} - 1)(aw_{opt} + aw_{min} - 2aw)]}$

^{1/2} Ratkowsky et al., 1983; ^{3/4} Huang and Hwang, 2011; ⁵ Rosso et al, 1993; ^{6/7} Rosso et al, 1995; ⁸ Presser et al. 1997; ^{9/10} Rosso and Robinson, 2001

Tab.16. Two flora competition growth models included in Microrisk Lab

Name	Formula
Jameson - No lag Buchanan model ¹	$\begin{cases} y_1(t) = \begin{cases} y_1 + \frac{\mu_{max1}}{\ln 10} t, & t < t_{max} \\ y_1 + \frac{\mu_{max1}}{\ln 10} t_{max}, & t \geq t_{max} \end{cases} \\ y_2(t) = \begin{cases} y_2 + \frac{\mu_{max2}}{\ln 10} t, & t < t_{max} \\ y_2 + \frac{\mu_{max2}}{\ln 10} t_{max}, & t \geq t_{max} \end{cases} \end{cases}$
Jameson - Buchanan model ²	$\begin{cases} y_1(t) = \begin{cases} y_1, & t < t_{lag1} \\ y_1 + \frac{\mu_{max1}}{\ln 10} (t - t_{lag1}), & t_{lag1} \leq t < t_{max} \\ y_1 + \frac{\mu_{max1}}{\ln 10} (t_{max} - t_{lag1}), & t \geq t_{max} \end{cases} \\ y_2(t) = \begin{cases} y_2, & t < t_{lag2} \\ y_2 + \frac{\mu_{max2}}{\ln 10} (t - t_{lag2}), & t_{lag2} \leq t < t_{max} \\ y_2 + \frac{\mu_{max2}}{\ln 10} (t_{max} - t_{lag2}), & t \geq t_{max} \end{cases} \end{cases}$

* The inferior number 1 or 2 in competition growth models represent the flora type.

^{1/2} Vimont et al., 2006

Tab.17. Ordinary differential equations for growth/ inactivation included in Microrisk Lab

Name	Formula
Non-isothermal growth models	
Baranyi - Cardinal parameter model ¹	$\begin{cases} \frac{dY}{dt} = \mu_{max} \left[\frac{1}{1 + \exp(-Q)} \right] [1 - \exp(Y - Y_{max})] \\ \frac{dQ}{dt} = \mu_{max} \\ Q = \ln \frac{q}{1-q} \\ Y(0) = Y_0 \\ q(0) = q_0 \\ \mu_{max} = \frac{\mu_{opt}(T-T_{max})(T-T_{min})^2}{[(T_{opt}-T_{min})(T-T_{opt})-(T_{opt}-T_{max})(T_{opt}+T_{min}-2T)](T_{opt}-T_{min})} \end{cases}$
Huang - Cardinal parameter model ^{2/3}	$\begin{cases} \frac{dY}{dt} = \mu_{max} \left[\frac{1}{1 + \exp(-4(t-t_{lag}))} \right] [1 - \exp(Y - Y_{max})] \\ t_{lag} = \frac{\exp(A)}{\mu_{max}^m} \\ Y(0) = Y_0 \\ \mu_{max} = \frac{\mu_{opt}(T-T_{max})(T-T_{min})^2}{[(T_{opt}-T_{min})(T-T_{opt})-(T_{opt}-T_{max})(T_{opt}+T_{min}-2T)](T_{opt}-T_{min})} \end{cases}$
Non-isothermal inactivation model	
Dynamic Weibull model ⁴	$\frac{dy}{dt} = -p \left(\frac{T-T_{ref}}{\delta_{ref}} \right)^p t^{p-1}, y(0) = y_0$
Dynamic Bigelow model ⁵	$\frac{dy}{dt} = -\frac{1}{D_{ref}} 10^{\frac{T-T_{ref}}{z}}, y(0) = y_0$

^{1/2/3} Huang, 2017; ⁴ Mafart et al, 2002; ⁵ Van Impe et al., 1992.

9 Statistical indicators in Microrisk Lab

To evaluate and compare the goodness of fit, the statistical indicator of residual sum of squares (RSS, Eq.1), mean square error (MSE, Eq.2), root mean square error (RMSE, Eq.3), regular Akaike information criterion (AIC, Eq.4, Akaike, 1974), modified AIC (AICc, Eq.5, Burnham & Anderson, 2003) and Bayesian information criterions (BIC, Eq.6, Schwarz, 1978) are provided such in the 'Model Evaluation' tab for all regression analyses. The coefficient of determination (R-square R², Eq.7) and adjusted coefficient of determination (Adjusted R², Eq.8) were provided only for linear models.

$$RSS = \sum_{i=1}^n (y_i - \hat{y}_i)^2 \quad \text{Eq.1}$$

$$MSE = \frac{RSS}{n-k} \quad \text{Eq.2}$$

$$RMSE = \sqrt{MSE} \quad \text{Eq.3}$$

$$AIC = -2 \log(\hat{\theta}) + 2k \quad \text{Eq.4}$$

$$AIC_c = AIC + \frac{2k(k+1)}{n-k-1} \quad \text{Eq.5}$$

$$BIC = -2 \log(\hat{\theta}) + k \ln(n) \quad \text{Eq.6}$$

$$R^2 = \frac{\sum_{i=1}^n (\hat{y}_i - \frac{1}{n} \sum_{i=1}^n y_i)^2}{\sum_{i=1}^n (y_i - \frac{1}{n} \sum_{i=1}^n y_i)^2} \quad \text{Eq.7}$$

$$\text{Adjusted } R^2 = 1 - (1 - R^2) \frac{n-1}{n-k-1} \quad \text{Eq.8}$$

where y_i is the i th value of the observation; \hat{y}_i is the i th value of the prediction; k is the number of parameters; and n is the number of sample data; $\log(\hat{\theta})$ is the numerical value of the log-likelihood for the fitted model (the probability of the data given a model in the model).

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